PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 6395-67856	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/US2004/011022	International filing date *(day/month/year)* 08.04.2004	Priority date *(day/month/year)* 11.04.2003
International Patent Classification (IPC) or national classification and IPC G01N33/569, C07K14/16		
Applicant THE GOVERNMENT OF THE UNITED STATES OF AM... et al		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
28.06.2005	01.09.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Giry, M Telephone No. +49 89 2399- 7328

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US2004/011022

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-26 as originally filed

   Sequence listings part of the description, Pages

   1-7 as originally filed

   Claims, Numbers

   1-40 as originally filed

   Drawings, Sheets

   1/3-3/3 as originally filed

   ☒ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/US2004/011022

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-40
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-40
Industrial applicability (IA)	Yes:	Claims	1-40
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Supplemental Box relating to Sequence Listing

Continuation of Box I, item 2:

1. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this report has been established on the basis of:

   a. type of material:

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☒ in written format

   ☒ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed

   ☐ filed together with the international application in computer readable form

   ☒ furnished subsequently to this Authority for the purposes of search and/or examination

   ☒ received by this Authority as an amendment on

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional observations, if necessary:

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 - Reference is made to the following **documents** :

D1: Simon F. et al. : "Synthetic peptide strategy for the detection of and discrimination among highly divergent primate lentiviruses." AIDS Res. Hum. Retroviruses, vol. 17, no. 10, 1 July 2001, pages 937-952

D2: Kim P. et al. : "Comparing tandem repeats and multiple antigenic peptides as the antigens to detect antibodies by enzyme immunoassay." J. Immunol. Meth., vol. 257, 1 November 2001, pages 51-54

2 - **Novelty** - Art. 33(1) and (2) PCT :

None of the available prior art documents disclose multiple antigenic peptides comprising a "core matrix" and at least two linear antigenic sequences bounded thereto wherein the linear antigenic sequence comprises *less than 16 amino acid residues* from the immunodominant region (IDR) of the transmembrane protein gp41 or gp36 of a *simian* immunodeficiency virus (claims 30 and 31), or from the V3 region of the envelope protein gp120 of a *simian* immunodeficiency virus (claim 32), and diagnostic methods (claims 1-25 and 35, 37 and 39-40), enzyme immunoassays (claims 26-29 and 36 and 38) and diagnostic kits (claims 33-34) containing both of them. The subject-matter of claims 1-40 can therefore be considered as novel.

3 - **Inventive step** - Art. 33(1) and (3) PCT :

3.1 Document D1 which is considered to represent the closest prior art document discloses detection and discrimination among divergent primate lentiviruses by two indirect ELISA methods using synthetic peptides mapping the gp41/36 region (detection component) and the V3 region (differentiation component) of four lentiviruses lineages (p. 939, Table 1). In the human field evaluation panel, the gp41/36 component correctly identified all the test samples with 98% specificity. Addition of a V3 SIVrcm peptide discriminated all the SIVrcm-positive samples.

This combined ELISA system is highly sensitive and specific for anti-lentivirus antibodies directed against HIV and SIV in human and nonhuman primate samples (Abstract).
The subject-matter of the present application differs from the teaching of document D1 in the number of amino acid residues constituting the antigenic portion of the synthetic peptides used for the detection.
The problem to be solved by the present application can therefore be seen in providing an alternative diagnostic method for the detection and lineage differentiation of primate lentiviruses and synthetic peptides therefor.

3.2 Document D2 teaches the use of tandem repeats and multiple antigenic peptides (MAPs) to improve the assay sensitivity by eliminating the problems associated with monomeric short peptides, and discloses a comparison between tandem repeats and MAPs as antigens for detecting antibodies by enzyme immunoassay. The model peptide system is derived from the consensus subtype B, V3-loop sequence of HIV-1 gp120. The monomeric peptide (M1) has *13 residues*. Peptides TR2 to TR5 are two to five tandem repeats of M1, respectively and peptides MAP2, MAP4 and MAP8 are multiple antigenic peptides composed of two, four and eight branches of M1, respectively (p. 52, col. 1, first paragraph). Document D2 demonstrates that poor analytical sensitivity of peptide-based enzyme immunoassays that use short monomeric peptides as the antigen can be improved significantly without sacrifying the assay specificity by using tandem repeats of MAPs.

3.3 The use of tandem ("at least two linear antigenic peptide") peptide is described in document D2 as providing the same advantages as in the present application. The skilled person would therefore regard it as a normal design option to include this feature in the methods described in document D1 in order to solve the problem posed.
The diagnostic method as featured in claims 1-25, 35, 37 and 39-40 and the enzyme immunoassays according to claims 26-28, 29, 36 and 38 can therefore not be considered as involving an inventive step.

3.4 The same comment hold true for the detection MAPs as featured in claims 30 and 31 and for the differentiation MAPs as featured in claim 32, and the kits containing

the same (claims 33-34).

4 - **Industrial applicability** - Art. 33(1) and (4) PCT :

The subject-matter of claims 1-40 appears to be industrially applicable.

Re Item VIII

Certain observations on the international application

1. The expression "core matrix" has no precise meaning and the description does not contain any information about the meaning intended for it. The set of claims as a whole is therefore considered to lacks clarity (Art. 6 PCT).

2. The vague and unclear term "about" used in claims 1, 11, 26, 28, 29 and 33 in relation to the number of amino acid residues constituting the "linear antigenic sequence" has no well-recognised meaning and leaves the reader in doubt as to the meaning of the technical feature to which it refers, thereby rendering the definition of the subject-matter of said claims unclear (Art. 6 PCT).